

REMARKS

Applicant has amended the specification and presented new claims 27 through 46 for entry.

Applicant has amended the specification to add the continuation data and to add the sequence identifiers that correspond to the sequence listing. Applicant has also corrected certain typographical errors. At page 5, line 28, the ending nucleotide of the nucleotide sequence encoding the gag gene product is changed from 2245 to 2235. The support for this correction is at Figure 5b, line 8, showing that the end of the gag gene is at the nucleotide position 2235 rather than 2245. At page 12, lines 7 and 8, the beginning of the U3 region of the long terminal repeat is changed from nucleotide 7845 to nucleotide 7842. The support for this amendment can be found at page 3, line 24, and from Figure 1a.

Applicant has cancelled claims 2 to 26 and hereby presents claims 27 through 46. Applicant submits that the newly presented claims are supported throughout the specification, including at page 4, lines 32-37; page 6, lines 22-25; pages 9-11; and page 27.

Applicant hereby requests that the sequence listing entered in the parent case be entered into this continuation application.

Applicant requests entry and consideration of this Preliminary Amendment. Applicant requests that the examiner assigned to the case contact Applicant's representative if prosecution may be assisted.

Respectfully submitted,
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VERSION WITH MARKINGS TO SHOW CHANGES MADE

The paragraph beginning at page 3, line 8, has been amended as follows:

According to a first embodiment, the object of the invention is a recombinant retroviral vector for the cloning and/or express and/or transfer of an exogenous nucleotide sequence, characterized in that it consists of any sequence contained in the ClaI-PvuII fragment situated approximately between nucleotides 7702 and 1527 (SEQ ID NO: 13) of the sequence given in Figure 1 and comprising the LTR sequence included between nucleotides 7842 and 144, the PBS site starting at nucleotide 145, the packaging sequence included in the sequence of 250 nucleotides following the end of the LTR sequence, the said sequence being capable of controlling the cloning and/or expression and/or transfer of the exogenous sequence.

The paragraph beginning at page 3, line 19, has been amended as follows:

According to another embodiment of the invention, the recombinant vector is characterized in that it consists of any sequence contained in the ClaI-BamHI fragment comprising the nucleotides 7702 to 310 (SEQ ID NO: 13) of the sequence shown in Figure 1, and comprising the LTR sequence included between the nucleotides 7842 and 144, the PBS site starting at nucleotide 145, the packaging sequence included in the sequence of 250 nucleotides following the end of the LTR sequence, the said sequence being capable of controlling the cloning and/or expression and/or transfer of the exogenous sequence, whatever its transcriptional orientation with respect to the transcriptional orientation of the virus.

The paragraph beginning at page 3, line 30, has been amended as follows:

According to this second embodiment of the invention, the vector is thus a retroviral vector for the cloning and/or expression and/or transfer of an exogenous nucleotide sequence consisting of any sequence contained in the ClaI-BamHI fragment situated approximately between nucleotides 7702 and 310 (SEQ ID NO: 13) of the

sequence given in Figure 1, the said sequence having the capacity to control the cloning and/or expression and/or transfer of the exogenous sequence.

The paragraph beginning at page 4, line 17, has been amended as follows:

According to an attractive embodiment of the invention, the recombinant vector is characterized in that it consists of all of the ClaI-PuvII fragment, comprising nucleotides 7702 to 1527 (SEQ ID NO: 11) of the sequence shown in Figure 1.

The paragraph beginning at page 4, line 21 has been amended as follows:

Another preferred retroviral vector consists of all of the ClaI-BamHI fragment (7702 to 310) (SEQ ID NO: 13).

The paragraph beginning at page 5, line 16, has been amended as follows:

Preferably the recombinant vector additionally comprises a part of the gag sequence situated between the nucleotides 619 and [2245] 2235 (SEQ ID NO: 14) of the sequence shown in Figure 5, in particular the sequence included between nucleotides 619 and 1527 (SEQ ID NO: 15) of the sequence shown in Figure 1.

The paragraph beginning at page 6, line 21, has been amended as follows:

A useful vector of the invention lacking the envelope sequence [consists] consisting of the fragment comprising nucleotides 7806 to 1527 (SEQ ID NO: 12) of the sequence shown in Figure 1.

The paragraph beginning at page 6, line 24, has been amended as follows:

The invention also relates to a recombinant vector such that the sequence contained in the ClaI-PvuII fragment (7702-1527) (SEQ ID NO: 11) and/or this fragment and/or the sequence contained in the fragment ClaI-BamHI (7702-310) (SEQ ID NO: 13) and/or this fragment is replaced either by a sequence hybridizing under conditions of high stringency with the sequence corresponding to the above-mentioned fragments or by a sequence having an at least 95% nucleotide homology with the sequence corresponding to the above-mentioned fragments or at least 85% homology in the case of the U3 sequence.

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The paragraph beginning at page 12, line 1, has been amended as follows:

Other characteristics and advantages of the invention will become apparent in the examples and Figures which follow.

Figure 1: Sequence of viral DNA used for the construction of the vector FOCH29.

Figure 2: A: Restriction map of the vector FOCH29.

References Seq "FB29"

Cla ----> U3 140 (7702-[7845]7842)

U3 ----> R410 ([7845]7842-8255)

R ----> CBS 145 (0-145)

PvuII ----> BamHI 208

PvuII ----> PvuII 1098

PvuIIMT ----> PvuII 1669

BsmAI ----> 55/150/765/1766/2531/2684

The paragraph beginning at page 15, line 9, has been amended as follows:

The oligonucleotide sequences used are:

1°) - for the first pair:

5' CTGCTGACGGGAGAAGAAAAAC-3' (SEQ ID NO: 3)

5' CCCGCTCAGAAGAACTCGTC-3' (SEQ ID NO: 4)

2°) - for the second pair:

5' GACGAGTTCT TCTGAGCGGG-3' (SEQ ID NO: 5)

5' GATCTGAACT TCTCTATTCTTG-3' (SEQ ID NO: 6)--

The paragraph beginning at page 28, line 5, has been amended as follows:

The viral integration was investigated by molecular methods, in particular by PCR using the following primers: oligo-SENSE situated in the beta-galactosidase gene with the following sequence: 5'- CGA CTC CTG G AG CCC GTC AGT ATC-3' (SEQ ID NO: 7); oligo-ANTISENSE situated in the viral LTR, overlapping between R and the start of U5 (LTR-508): 5'- CAG CGA GAC CAC GAG TCG GAT GC-3' (SEQ ID NO: 8) in a region which has been prepared by EspI/BssHII deletion.

The paragraph beginning at page 29, line 4, has been amended as follows:

The construction was made from the plasmid pUC19 including the EcoRI-PvuII fragment described in part B1-1: enzymatic cutting by the restriction enzyme EspI (or IsoCelII) at position 7864 (namely +23 of the viral LTR). At the 5' end the bases generated by a EcoRI cut were artificially added to a double stranded synthetic oligonucleotide complementary to the 23 bases of the LTR (140 bases, 103 of which are bases of the envelope). At the 3' end the oligonucleotide is complementary to the cohesive SpeI ends. The oligonucleotide sequences are the following: oligo-SENSE 5' - AAT TCA ATG AAA GAC CCC AAA TTG C-3' (SEQ ID NO: 9), oligo-ANTISENSE 5' - TAA GCA ATT C GG TGG GGT CTT TCA TTG-3' (SEQ ID NO: 10).

The paragraph beginning at page 30, line 1, has been amended as follows:

In this perspective of improving viral safety, an alternative construction was prepared in which the GAG of FB29 is cut at the unique AhaIII (or isoDraI) site at position 1031 (SEQ ID NO:16); only a quarter of the GAG sequences are then conserved. The cut generated by AhaIII having blunt ends as for PvuII used for the cloning of FOCH29, the construction was made exactly superposable, the cloning upstream not being modified; downstream, the blunted ended SmaI site of the polylinker of pUC19 was used.